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CASTELLE FILE

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Tribufos (DEF®), Acute oral toxicity rat.
Sulfon metabolite, Acute oral toxicity rat.

TO: Bruce Sidwell PM-53
Reregistration Branch
Special Review and Reregistration Division (H7508C)

3/1/93

FROM: Robert P. Zendzian Ph.D.
Senior Pharmacologist
Toxicology Br II
Health Effects Division (H7509C)

THROUGH Karl Baetcke Ph.D.
Chief
Toxicology Br II
Health Effects Division (H7509C)

Karl D. Baetcke 3/1/93

Compound; Tribufos (DEF®) Tox Chem #864

Registration #074801 Registrant; Miles

MRID # 419549-03 DP barcode; D180867
424081-01

Action Requested

Review the following studies;

1) Acute Oral Toxicity with Technical grade tribufos (DEF®) in rats, L.P. Sheets, Mobay, Study No 90012-ES, Report # 100697, May 20, 1991, MRID 419549-03

Core Classification Acceptable

Conclusion

Doses tested and mortality: Males 294 (0/5), 429 (3/5) & 552 mg/kg LD_{50} between 294 and 429 mg/kg; Females 192 (0/5), 235 (4/5) & 294 (4/5) mg/kg, LD_{50} between 192 and 235 mg/kg. Signs of toxicity at all doses (deceased activity, lacrimation, nasal discharge, salivation, diarrhea, tremor, convulsions). Deaths occured within seven days after dosing. Computer

program used for calculating lethality parameters appears to be invalid. Toxicity catagory II

2) Experimental Acute Oral Toxicity with HBM sulfone (a metabolite of Tribufos, DEF®) in female rats. A.B. Astroff & S.D. Phillips, Miles, Study No 92-912-OD, Report # 102684, June 18, 1992, MRID 424081-01

Core Classification Acceptable

Conclusion

Doses tested 2000 mg/kg in females (most sensitive sex for parent compound). No toxicity observed. LD_{50} >2000 mg/kg Toxicity catagory IV

cc
CBRS

Attachments
DERs
one-liners

Data Evaluation Report

Compound Tribufos (DEF)

Citation
Acute Oral Toxicity with Technical grade tribufos (DEF®) in rats, L.P. Sheets, Mobay, Study No 90012-ES, Report # 100697, May 20, 1991, MRID 419549-03

2/11/93

Reviewed by Robert P. Zendzian Ph.D.
Senior Pharmacologist
Health Effects Division

Core Classification Acceptable

Conclusion

Doses tested and mortality: Males 294 (0/5), 429 (3/5) & 552 mg/kg LD_{50} between 294 and 429 mg/kg; Females 192 (0/5), 235 (4/5) & 294 (4/5) mg/kg, LD_{50} between 192 and 235 mg/kg. Signs of toxicity at all doses (deceased activity, lacrimation, nasal discharge, salivation, diarrhea, tremor, convulsions). Deaths occured within seven days after dosing. Computer program used for calculating lethality parameters appears to be invalid. Toxicity catagory II.

Materials

Technical grade Tribufos
Clear pale yellow liquid
Reference No; 85R-26-39
Purity 98.1%

From Mobay Ag Chemicals Division

Male and female Sprague-Dawley rats (Sas:CD(SD)BR) from Sasco Houston TX

Experimental Design

Animals were administered a single oral dose in corn oil. The experimental design and resulted are summarized in Table 1 from the report.

Observations

Animals were observed daily for mortality and toxicity for 14 days after dosing. Body weights were taken as shown in Table 1. All animals that died on test were necropsied. Survivors were sacrificed by CO_2 asphyxiation on day 14 and necropsied.

LD_{50} values, 95% confidence intervals and the slope of the mortality curves were calucalted using a statistical program obtained from the EPA, Duluth Mn.

Results

Mortality, toxicity and body weight data are sumarized in Table 1 from the report.

Signs of toxicity were typical of organophosphate toxicity and consisted of decreased activity, lacrimation, nasal discharge, salivation, diarrhea, tremor, convulsions and death. All deaths occured within seven days after dosing.

Lethality parameters were calculated as follows;

	LD_{50}	95% confidence limits	Slope
Males	435 mg/kg	(302-581 mg/kg)	10.6
Females	234 mg/kg	(183-296 mg/kg)	13.4

Dscussion

The results obtained in this study were not sufficient to allow calculation of an LD_{50} or the other parameters calculated. This conclusion is based on the actual mortality data obtained and the degrees of freedom for each sex. The male data have mortality values of 0%, 60% and 80% indicating that the LD_{50} most likely lies between the low dose and the intermediate dose (294 and 429 mg/kg respectively). Plotting this data on log/probit paper gives an LD_{50} of 380 mg/kg and indicates 28% mortality at the low dose of 294 mg/kg. Nothing better can be done with the male data.

The female data is even less useful. Mortality values are 0%, 80% and 80% again indicating that the LD_{50} most likely lies between the low dose and the intermediate dose (192 and 235 mg/kg respectively). Since the two doses which produced mortality produced the same percent mortality, the data cannot be plotted.

It is apparent that the computerized calculations are invalid as is the program.

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Data Evaluation Report

Compound HBM sulfone [plant metablite of Tribufos (DEF)]

Citation
Experimental Acute Oral Toxicity with HBM sulfone (a metabolite of Tribufos, DEF®) in female rats. A.B. Astroff & S.D. Phillips, Miles, Study No 92-912-OD, Report # 102684, June 18, 1992, MRID 424081-01

3/16/93

Reviewed by Robert P. Zendzian Ph.D.
Senior Pharmacologist
Health Effects Division

Core Classification Acceptable

Conclusion

Doses tested 2000 mg/kg in females (most sensitive sex for parent compound). No toxicity observed. LD_{50} <2000 mg/kg Toxicity catagory IV

Materials

HBM sulfone
viscus liquid, white solid after refrigeration
Reference number, Standard K-424
Purity 100%

Female Sprague-Dawley rats (Sas:CD(SD)BR) from Sasco

Experimental Design

Five female rats were given orally, either vehicle (water) or 2000 mg/kg HBM sulfone in water.

Observations

Animals were observed twice daily for 14 days after dosing. Animals were weighed prior to dosing and on days 7 and 14.

Results

No signs of compound related toxicity were observed. The LD_{50} of HBM sulfone is greater than 2000 mg/kg.

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Chemical:	**S,S,S-Tributyl phosphorotrithioate**
PC Code:	**074801**
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